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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): INRP:041US

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

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Signature: /Travis Wohlers/

Typed or printed name: Travis M. Wohlers

Application Number	Filed
08/758,033	November 27, 1996

First Named Inventor: Gary L. Clayman

Art Unit	Examiner
1632	Wu Cheng Winston Shen

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 57,423.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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02/22/08
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

ARGUMENTS IN SUPPORT OF THE REQUEST FOR PRE-APPEAL BRIEF REVIEW FOR APPLICATION SERIAL NO. 08/758,033

The present rejection against the claims 1-9, 11-14, 16-19,26,36,37, and 146-150 for anticipation by U.S. Patent No.5,496,731 to Xu *et al.* as evidenced by U.S. Patent No.6,590,086 to Fung et al. and Donehower *et al.* (The Cancer Bulletin 46: 161-166 (1994)) arise from common factual deficiencies in the examiner's understanding of the teachings of the '731 patent. Xu is concerned with a broad-spectrum tumor suppressor gene and the protein expressed by that gene," which is a ***retinoblasoma protein of about 94 kD ($p94^{RB}$)*** (Xu, Abstract) and is not p53. In contrast, the present claims are directed to methods of inhibiting growth of or inducing apoptosis in a tumor cell expressing wild-type p53 in a human subject. These methods comprise parenterally administering a viral expression construct encoding a functional ***p53 polypeptide*** to the subject. The examiner has failed to establish that Xu teaches such a method.

The treatments contemplated by Xu are described as using a ***$p94^{RB}$ expression vector or $p94^{RB}$ protein*** (Xu, Abstract). The examiner alleges that in column 11, lines 25-33, Xu teaches an embodiment in which the tumor or cancer cells are cells having no detectable genetic defect of a tumor suppressor gene, which may be a p53 gene (Final Action, p. 8). However, these statements from Xu are made only in the context of treatment with ***$p94^{RB}$*** and not p53 (*see* Xu, Summary of the Invention). In other words, there is no mention of inhibiting growth of or inducing apoptosis in a tumor cell expressing wild-type p53 in a human subject using a viral expression construct encoding a functional p53 polypeptide.

It appears that Xu's only mention of p53 therapies is in Background section 1.3.3.3. Xu uses this section to point out alleged deficiencies in both p53 and RB^{110} therapies that Xu's $p94^{RB}$ therapy is said to overcome. In particular, Xu notes that : "Tumor cell lines deleted for p53 have been successfully treated with wild-type p53 vector to reduce tumorigenicity. However, the introduction of either p53 or RB^{110} into cells that have not undergone lesions at

these loci does not affect cell proliferation." (Xu, col. 5, ln. 21-26) (citations omitted). This clearly does not teach a method of inhibiting growth of or inducing apoptosis in a tumor cell expressing ***wild-type p53*** according to the methods recited in the current claims. In fact, it teaches away from such an approach.

Accordingly, the examiner fails to establish a *prima facie* case of anticipation because Xu does not teach or suggest a method as recited in the current claims.

Finally, the examiner maintains the provisional double-patenting rejection of claims 1-14, 16-20, 26-32,36,37 and 146-150 over claims 26,29,58,89 of co-pending Application No. 09/968,958 (the '958 application). If the above-mentioned anticipation rejection is overcome and a provisional double-patenting rejection is the only rejection remaining in the application, the examiner should withdraw the rejection and permit the application to issue a patent. Once either the present application or the '958 application issues as a patent, a terminal disclaimer will be filed, if appropriate, in the remaining pending application.